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Endoscopic characteristics and management of Subepithelial Lesions in Video-Gastascopies

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Abstracts

Background: Subepithelial lesions (SELs) are incidental findings on endoscopies. Some have evil potential.

Aim: Assess the prevalence, endoscopic characteristics, and diagnostic/therapeutic management of Sub-epithelial lesions (SELs) in video-gastroscopies (VGC).

Materials and methods: All VGC for January 2011-June to 2020 were included, and cases with missing data were excluded. The following was recorded where a SELS was identified: indication, age, sex, size, location and histology, findings from endoscopic ultrasonography (EUS), fine needle aspiration (FNA), and surgical resection.

Results: 55 SELS were evidenced in 7,983 patients (0.7%). 72% were women; the most common indication was dyspepsia (26%). The most frequent location was in the stomach (74%). The mean size was 16 mm (5-50 mm), and half were smaller than 10 mm. Seven presented ulcerated mucous, four were in the gastric body, and 86% were referred for gastrointestinal bleeding/anemia. In 26 cases, 55 (48%) standard biopsies were performed, and 6 of the 55 (11%) biopsies on biopsies, with no diagnostic yield. EUS was performed in 11% of them, all larger than 10 mm: 2 ectopic pancreases, one lesion-compatible leiomyoma, two lesions of the muscularis propria (leiomyoma / GIST), and one extrinsic compression. No FNA was performed. All LSEs were managed conservatively.

Conclusions: This is the first national study on the prevalence of SELS in the upper gastrointestinal tract and was comparable to other series. The diagnostic yield of the biopsy was null. In most cases, the lesions were managed according to the recommendations of international guidelines.

Keywords: Pancrelipase; Endosonographic; Gastrointestinal Stromal Tumors; Gastrointestinal Hemorrhage

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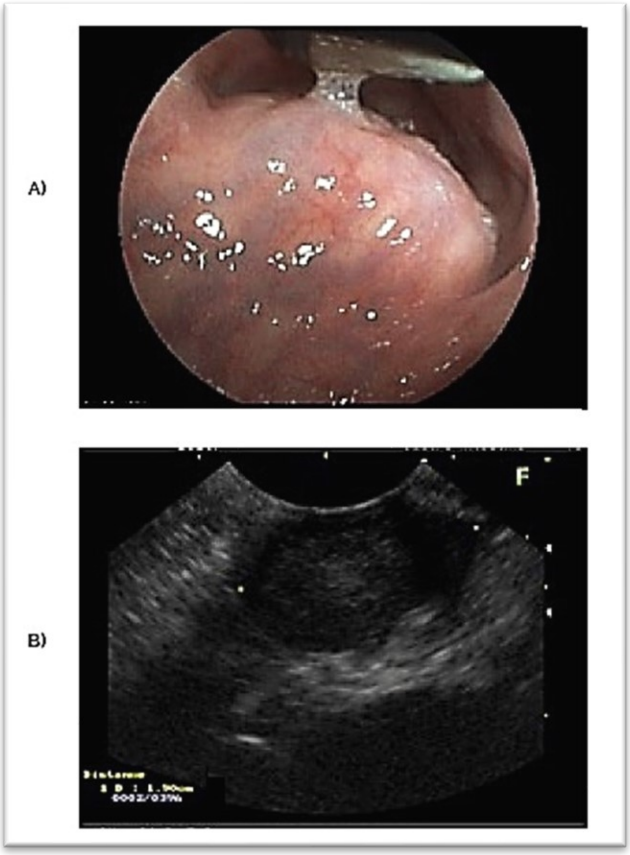
Introduction

Conceptually, subepithelial lesions (SELs) originate in the deeper layers of the gastrointestinal tract wall (GIT). In order of frequency, they are located in the stomach, esophagus, and duodenum [1]. Most are covered by healthy mucosa; however, inflamed or ulcerated mucosa is occasionally observed 2 (Figure 1).



Source: self-made.

Figure 1: A) Subepithelial lesion in the esophagus. B) Subepithelial lesion in the esophagus assessed by EUS.

It is relatively common to find these injuries in routine GCV. The epidemiological data are imprecise, but approximately one in every 300 routine digestive endoscopies reveals a bulging of the gastrointestinal wall, covered by mucosa with a normal endoscopic appearance, suggestive of SEL [2]. There is excellent diagnostic difficulty in differentiating the type based on its endoscopic appearance. In general, biopsies of the overlying mucosa do not provide a definitive histological diagnosis [3-6].

Since LSEs are an incidental finding in most cases, some issues become relevant. First, it is necessary to differentiate them from extrinsic compressions, which, unlike SELs, do not originate within the GIT wall. Second, it is necessary to determine the risk that this lesion is malignant.

Among the benign SELs, the following stand out: lipomas, ectopic pancreas, varicose veins, and leiomyomas [7]. Some rare lesions resemble SELs, such as esophageal duplication cysts, inflammatory fibroid polyps, and granule cell tumors [8].

Carcinoid and stromal tumors (GIST) are malignant or potentially malignant SELs. The latter represents about 80% of mesenchymal tumors and is more frequent in the upper GIT [9,10].

Although VGC performs the initial diagnosis of these lesions, the USE can provide important information such as the precise size, the source layer, the echogenicity, the boundaries, and the shape of the lesions [11]. EUS is the test of choice to characterize SELS. Still, it provides a conclusive diagnosis in limited lesions, such as varicose veins, ectopic pancreas, and lipoma, which present specific ultrasound characteristics.

In other situations where there is diagnostic doubt, such as in cases of leiomyomas and GIST and / or suspicion of malignancy, a cytological and / or histological examination is necessary. These can be performed through biopsy techniques, biopsies on biopsies, macro-biopsies, and/or fine needle puncture. The biopsy-on-biopsy approach shows a diagnostic yield of around 33% for lesions smaller than 1 cm and 46% for lesions greater than 1 cm, with better results in lesions located in the esophagus than in those found in the stomach and duodenum. The main complication is bleeding, which occurs in 14% of cases [11]. Macro-biopsies show satisfactory results in around 80%. Still, with higher rates of bleeding and perforation complications, EUS-guided FNA has emerged as a minimally invasive and safe method for acquiring samples, mainly in lesions where GIST is suspected. However, its performance is debated and is affected by several factors, among which size stands out—injury [12, 13].

Aim:

To assess the prevalence of subepithelial lesions of the upper GIT in patients who underwent VGC in the Gastroenterology Clinic. Describe subepithelial lesions' endoscopic and histological characteristics and their diagnostic and therapeutic management.

MATERIALS AND METHODS:

It is a cross-sectional, descriptive, and retrospective study. The reports and requests of all the VGC of patients 18 years of age or older, of both sexes, were included in a period from January 2013 to June 2020 carried out at the Gastroenterology Clinic of the Alkarama hospital Baghdad, Iraq.

Partial VGC due to intolerance or missing data and those performed more than once in the same patient were excluded from the analysis. By endoscopic report and review of the clinical history, in the cases where SELs were identified, the following variables were considered:

a) Presence of SELs defined as a protrusion or bulging of the wall of the digestive tract lined with mucosa, with common characteristics, which does not change with changes in the patient's position:

b) Sex

c) Age

d) Indication of the VGC

e) Location of the LSE

f) Size of the LSE

g) Ulceration of the mucosa

h) Anatomopathological characteristics by biopsy

i) EUS and FNA result

j) Performing endoscopic resection

k) Carrying out surgical resection

The results obtained were entered into an anonymized database to guarantee privacy, and the study was carried out considering the framework of the Helsinki 2013 and CIOMS 2002 regulations.

To record the data, a data extraction table was prepared that included the study variables already described and was carried out by two specialist doctors who knew the terminology in the reports. In case of doubt, an independent professional performed a second extraction.

The data were analyzed using descriptive statistics (percentages, ranges, means, and standard deviations). The statistical package *EpiData* version 3.1 was used. (free software).

ETHICAL CONSIDERATIONS

All endoscopic studies were performed under the patients' informed consent, oral and written. The data obtained in these procedures were used to carry out the retrospective study, and confidentiality was guaranteed.

RESULTS

7,983 VGC performed from January 2011 to June 2020 were included, where 55 SELs were reported, corresponding to a prevalence of 0.7%.

From the analysis of the studies with an endoscopic diagnosis of SELs, 72% were women, the mean age was 64 years, and the main indication was dyspepsia (26%). The most frequent location of SELs was in the stomach (74%), followed by the duodenum (13%) and the esophagus (13%).

Of the 5 LSEs found in the esophagus, two were located in the middle third and 3 in the distal third, all greater than 10 mm. The etiological diagnosis was reached in one of them.

In the duodenum, 5 SELs were observed, all in duodenum II. Three were more significant than 10 mm, and the etiological diagnosis was not reached in any of them.

Among the lesions located in the stomach, approximately half of them were found in the antrum (43%), followed by the body (30%), the cardia (16%), and the fundus (11%).

The mean size of the LSE was 16 mm (range 5-50 mm); 50% were less than 10 mm, 27% were lesions between 10 mm and 20 mm, and 23% were greater than 20 mm. Seven (13%) presented ulcerated mucosa; two were in the duodenum and five in the stomach; the latter was in the gastric body (57%). The main reason for the indication for endoscopy in these cases was gastrointestinal bleeding/anemia (86%). It was possible to determine the etiology in none of the lesions with ulcerated mucosa.

Five (26%) of the 19 SELs surveyed in the antrum, located explicitly on greater curvature, presented central umbilication, which determined the endoscopic diagnosis of the ectopic pancreas. Standard biopsies were performed in 26 SELS (48%) and biopsies on biopsies in 6 SELs (11%), not obtaining a histological diagnosis in any patient. EUS was performed in 6 SELs (11%), five in the stomach and one in the esophagus, all greater than 10 mm. Of the gastric lesions, 2 were reported as ectopic pancreas, 2 as hypoechoic lesions in the muscular propria (GIST/leiomyoma), and extrinsic gastric compression due to splenomegaly. Esophageal SELs were reported as hypoechoic lesions in the muscular mucosae compatible with leiomyoma. No FNA, endoscopic, or surgical resection was performed. All LSEs were managed conservatively. As far as we know, this work is the first to evaluate the prevalence in the country and the region. The data found (0.7%) shows the variability of the prevalence between different areas since it was similar to the work of that done in South Korea (0.76%) [17]. Still, it was more than double that described by research in Sweden [18], where the prevalence was 0.3%. In more recent work in South Korea, the prevalence was 1.94%. In the latter, the authors justify that the more generalized use of VGC for gastric cancer screening in recent years may justify the higher detection of LSE [18].

On several occasions, gastroenterologists and surgeons are faced with endoscopy results that report SELs of the upper digestive tract, which raises questions about what to do next. In the same way, patients before the diagnosis of SELs are anxious while waiting for the resolution of the problem. The main concern in these cases is that the lesion found incidentally may correspond to SELs with malignant potentials, such as GIST, neuroendocrine or granular cell tumor.

Digestive endoscopy, in addition to the initial diagnosis of SELs, is capable of providing important information, such as size, the appearance of the mucosa that covers them, consistency, and other endoscopic signs that can predict the etiological diagnosis (pillow sign in lipomas or umbilication central in the ectopic pancreas), as well as in the differential diagnosis with extrinsic compressions, observing the possible alteration of its conformation with the change of decubitus of the patient.

SELs usually present with a normal-appearing mucosa with a similar coloration to the surrounding mucosa, although they can be ulcerated, as can occur in solid lesions such as GISTs. Another exception is when they present a central umbilication, typical of the ectopic pancreas [16]; according to the work of Mickuniene *et al.,* 90% of the lesions identified by endoscopy as ectopic pancreas presented central umbilication, which makes possible their presumptive endoscopic diagnosis in the face of this finding. In this study, three of the five SELs diagnosed as the ectopic pancreas (all located in the antrum) presented the typical appearance. The definitive diagnosis was made without the need for other studies. In the remaining two, the diagnosis was suggested by EUS[14].

The location of the injury can also help predict its nature. Esophageal SELs rarely have malignant potential (1%), unlike gastric and duodenal lesions, which have a risk of malignancy greater than 20% (18). In this study, none of the lesions in the esophagus was described as potentially malignant. The distribution of the 55 SELS in this study about the topography accessed by endoscopy showed that the most common location was the stomach (74%), the antrum being the most frequent sector (43%), which coincides with what was described in the literature [19].

EUS is often indicated to obtain other important information that can help to characterize better SELs, such as size, shape, echogenicity, and layer of origin. However, even with this information, doctors face injuries that raise doubts, as in the cases of injuries originating in the muscular propria, which may correspond to leiomyomas or GIST. The other ultrasound findings are similar in these cases and impede their distinction. In this work, two of the SELs evaluated by EUS originated in the muscular propria, and it was impossible to distinguish which of the two entities it was. Both lesions had a size (of 10 mm), for which they were managed conservatively, following international guidelines, not observing an increase in size in a follow-up period of 1 year (22,23). This low diagnostic yield suggests that EUS could be helpful in selected cases with lesions smaller than 10 mm, to rule out a differential diagnosis with esophageal or gastric varix or the staging of a known carcinoid tumor.

For the histological diagnosis of SELs, endoscopic methods can be used to acquire material. Among them, the following stand out: the technique of "biopsies on biopsies," macro biopsies, myomectomies, and submucosal resections. It is essential to highlight that these techniques can be used where EUS-FNA is unavailable. However, before performing the procedure, it is imperative that EUS previously evaluates the LSE to characterize them, thus reducing the possibility of complications [22].

The technique of "biopsies on biopsies" has been initially described for acquiring tissue from hypoechoic lesions of the fourth layer. However, some studies showed a low diagnostic yield of around 17% (22,24). In the study under discussion, this technique was performed in 11% of SELs, not achieving a histological diagnosis, which is consistent with the above.

The EUS-FNA sample minor complication rates with similar performance would be indicated when their diagnostic doubts lesions assessed by USE, such as hypoechoic lesions of the muscular which may have a different prognosis (leiomyoma, GIST or schwannoma) [22,23]. Due to the low number of EUS performed in this series, EUS-FNA was not completed due to a lack of indication.

Clinicians must decide between resection or follow-up when dealing with a subepithelial lesion. Surveillance with EUS or VGC is common in asymptomatic SELs patients with no signs of malignancy, although such an approach has not been formally validated. Because little is known about the natural course of SELs, the appropriate strategy for management remains controversial. Although it was not part of the objectives, it was found that endoscopic follow-up of the lesions was carried out in 5 cases, 3 were (at 10 mm and none of the latter changed their size or characteristics in 12 months

These findings, although descriptive, are consistent with previous studies that have suggested, given that the majority of small SELs ((10 mm) do not present changes that increase the suspicion of malignant potential in the medium term, a conservative policy with endoscopic surveillance it is a safe strategy [24,26].

According to a gradual approach to SELs, EUS is recommended for SELs > 10 mm, and histological evaluation with FNA for hypoechoic SELs less than 3 cm in diameter. Surgery for SELs greater than 3 cm with endoscopic ultrasound characteristics guiding GIST is recommended. Although these procedures help categorize a lesion, in most cases, they cannot determine the type of lesion or its benign or malignant nature [25]. Although the high-risk findings to predict malignancy of a GIST by EUS, such as heterogeneity, cystic changes, and calcifications, are used clinically, the studies that have evaluated their usefulness show that they are not very sensitive, being the size of the lesion the only one independent parameter that can predict malignancy in these lesions [25,27]. Clinicians must consider whether an invasive method is necessary, individual risk, and patient preference. Following these recommendations, all the lesions assessed by EUS were> 10 mm in this series. However, several lesions greater than 10 mm were not evaluated with this method since they presented endoscopic characteristics compatible with lipomas, ectopic pancreas, or extrinsic compressions because the equipment was not available due to technical problems or the patients did not attend, so it was not possible to achieve the etiological diagnosis in most of them.

This work presents the limitations of all retrospective work, and, in addition, it is emphasized that endoscopists with the same experience performed not all endoscopies. It was not specified in all cases in which area of the lesion the biopsies were taken or the same number. The size of the LSE was measured by visual estimation. Not all endoscopists used the same measurement technique, for example, comparing the lesion with open biopsy forceps, which could underestimate or overestimate their size.

However, this work has the strength of being the first in the field to evaluate the prevalence of SELs in the upper digestive tract and show its endoscopic characteristics and in EUS when possible. As in other series, this type of lesion evidenced poor diagnostic performance of biopsies.

CONCLUSIONS

This is the first national study on the prevalence of SELs in the upper gastrointestinal tract, comparable to the prevalence in other series. The diagnostic performance of the biopsy (standard and biopsy on biopsy) was null. In most cases, the lesions were managed according to the recommendations of international guidelines.

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